Review

Techniques used in orally disintegrating drug delivery system

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Abstract
Formulation of a convenient dosage form for administration, by considering swallowing difficulty and poor patient compliance, leads to development of orally disintegrating tablets. This are also called as orodisperse, mouth dissolving, rapidly disintegrating, and fast melt system. This disintegrates in the mouth in seconds without chewing and the need of water which is advantageous mainly for pediatrics, geriatrics and patients having difficulty in swallowing tablets and capsules. Conventional preparation methods are spray drying, freeze drying, direct compression, Molding, and sublimation while new technologies have been developed for the production of orodispersible tablets. This review depicts conventional and recent technologies that are used to prepare orodispersible tablets in detail.

Keywords: Orally disintegrating tablet; Superdisintegrant; Patented technologies; Orodispersible tablets

Introduction
Oral dosage forms like tablets and capsules possessing great problem of swallowing mainly for pediatrics, geriatrics, and bedridden, nauseous or non-compliant patients’. Orally disintegrating dosage forms has to be placed in mouth and then get dispersed in saliva without the need of water [1, 2]. Orally disintegrating tablets are also called as orodisperse, mouth dissolving, rapidly disintegrating, fast melt, and quick dissolve system. From past decade, there has been an increased demand for more patient-friendly and compliant dosage forms. As a result, the demand for developing new technologies has been increasing day by day [3]. United States Food and Drug Administration (FDA) define orally disintegrating tablets as “A solid dosage form which contain a medicinal substance or active ingredient which disintegrates rapidly within a matter of seconds when placed upon a tongue” [4]. US Food and Drug Administration Center for Drug Evaluation and Research (CDER) defines, in the ‘Orange Book’, an ODT as “a solid dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue”[5]. European Pharmacopoeia described orally disintegrating tablets as ‘uncoated tablets intended to be placed in the mouth where they disperse rapidly before being swallowed’ and as tablets which should disintegrate within 3 min [6]. About 35% of the general population in addition to 30-40% of elderly institutionalized patients and 18-22% of all persons in long term care facilities suffer from dysphagia, i.e. difficulty in swallowing [7]. Orally disintegrating tablets have been found to be the choice for Psychiatric as well as patient suffering from stroke, thyroid disorder, Parkinson’s diseases and multiple sclerosis, patients with nausea, vomiting and motion sickness [8].

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Advantages of an orally disintegrating drug delivery system [9, 10]

- Improved patient compliance.
- Rapid onset of action and may offer an improved bioavailability.
- Useful for pediatric, geriatric and psychiatric patients.
- Suitable during traveling where water is may not be available.
- No specific packaging required, can be packaged in push through blisters.
- Smooth mouth feel and pleasant taste.
- Conventional manufacturing equipment.
- Cost effective.
- Good chemical stability as conventional oral solid dosage form.

Characteristics of an ideal orally disintegrating drug delivery system [10]

Orally disintegrating drug delivery system should possess following characteristics:

- Utilizes cost effective production method.
- Require no water for oral administration.
- Dissolve / disperse/ disintegrate in mouth in a matter of seconds.
- Have a pleasing mouth feel and taste masking.
- Less friable and have sufficient hardness.
- Leave minimal or no residue in mouth after administration.
- Manufacturing using conventional manufacturing method.

Choice of drug candidate [3]

Suitable drug candidate for orally disintegrating tablet should possess:

- No bitter taste.
- Good stability in water and saliva.
- Dose should be low as possible.

Unsuitable drug candidate for orally disintegrating tablet should include:

- Short half-life and frequent dosing.
- Drug having very bitter taste.
- Required controlled or sustained release.

Taste masking

Taste masking is very essential so as to mask the bitter taste of most of the drugs. Number of techniques are developed for masking the bitter taste of most of the drugs, that includes formation of pellets by extrusion, spherization or mass extrusion [11], coating of drug using a taste masking polymer [12, 13], spray drying the drug dispersed in a polymeric solution [14], complexation of drug by inclusion in cyclodextrin [15, 16], drug-resinate complex formation [17, 18], microencapsulation of drug by polymer [19].

Techniques in preparation of orally disintegrating drug delivery system

The various technologies are developed for the preparation of Orally Disintegrating Drug Delivery System that are:

- Freeze drying
- Spray drying
- Molding
- Phase transition process
- Melt granulation
- Sublimation
- Mass Extrusion
- Cotton Candy Process
- Direct compression

Freeze drying

Lyophilization means drying at low temperature under condition that involves the removal of water by sublimation. Drug in a water soluble matrix which is then freeze dried to give highly porous structure. The tablets prepared by lyophilization disintegrate rapidly in less than 5 seconds due to quick penetration of saliva in pores when placed in the oral cavity. Lyophilization is useful for heat sensitive drugs i.e. thermo-labile substances [20, 21].

Ahmed et al. prepared lyophilized tablet using freeze drying technique. The lyophilized tablet prepared by dispersing drug Ketoprofen in aqueous solution of highly water soluble carrier consisting of gelatin, glycine and sorbitol in blister packs and then subjected to lyophilization in blister packs. It was found that the increase in solubility of ketoprofen from lyophilized tablet matrix was nearly three times greater than solubility of the plain drug which was due to supersaturation generated by amorphous form of drug [22].

Spray drying
 Spray drying can produce highly porous and fine powders that dissolve rapidly. This technique is based on a particulate support matrix, which is prepared by spray drying an aqueous composition containing support matrix and other components to form a highly porous and fine powder. This is then mixed with active ingredients and compressed into tablets. The formulations are incorporated by hydrolyzed and non-hydrolyzed gelatins as supporting agents, mannitol as a bulking agent, sodium starch glycolate or croscarmellose sodium as disintegrating and an acidic material (e.g., citric acid) and/or alkali material (e.g., sodium bicarbonate) to enhance disintegration and dissolution. Tablet compressed from the spray dried powder disintegrated within 20 seconds when immersed in an aqueous medium.

Allen et al. used a spray drying technique to prepare fast dissolving tablets. The tablets made from this technology are claimed to disintegrate within 20 seconds [23].

**Molding**

Tablets prepared by this method are solid dispersions. Molded tablets offer improved taste due to water-soluble sugars present in dispersion matrix.

Different molding techniques can be used to prepare mouth-dissolving tablets:

a. Compression molding: The manufacturing process involves moistening the powder blend with a hydro-alcoholic solvent followed by compressing into mold plates to form a wetted mass which is then air dried to remove the solvent. Such tablets are less compact than compressed tablets and possess a porous structure that hastens dissolution.

b. Heat molding: A molten matrix in which drug is dissolved or dispersed can be directly molded into orodispersible tablets. The tablets prepared using heat molding process involves settling of molten mass that contain a dispersed or dissolved drug [24]. In this process, the suspension or solution of drug, agar and sugar is prepared and then poured into the blister packaging. The agar solution is then solidified at room temperature to form a jelly and dried at 30 °C under the vacuum. Developed orally disintegrating tablets was found to improve the mouth feel due to the presence of the water soluble sugars [25].

c. No vacuum lyophilization: This process involves evaporation of solvent from a drug solution or suspension at a standard pressure. Molded tablets had less mechanical strength. Drug can be present as micro particles or discrete particles dispersed in the matrix. However, adding sucrose, acacia or polyvinyl pyrrolidone can increase mechanical strength. They possess highly porous structure which is supposed to increase their disintegration and dissolution rates [26].

**Phase transition process**

The combination of low and high melting point sugar alcohols, as well as a phase transition in the manufacturing process, is important for making orally disintegrating tablets without any special apparatus. Here, tablet produced by compressing the powder containing two sugar alcohols of high and low melting point and subsequently heating at temperature between their two melting points. Orally disintegrating tablets were produced by compressing powder containing erythritol (melting point: 122 °C) and xylitol (melting point: 93-95 °C), and then heating at about 93 °C for 15 min. After heating, the median pore size of the tablets was increased and tablet hardness was also increased. The increase of tablet hardness with heating and storage did not depend on the crystal state of the lower melting point sugar alcohol.

Kuno et al. studied the effect of preparation method on the properties of orally disintegrating tablets manufactured using phase transition of sugar alcohol. Before heating process, tablet did not have sufficient hardness because of low compatibility but after heating, increase in interparticular bonding or binding surface area occurs which then increased tablet hardness [27].

**Melt granulation**

Abdelbary et al. prepared orally disintegrating tablet by incorporating a hydrophilic waxy binder PEG 6-stearate (Superpolystate®) in the formulation. It has a melting point of 33-37 °C and HLB value of 9. It acts as a binder and increases the physical resistance of tablet. It helps for fast disintegration of tablet when place in mouth and leaving no residue in oral cavity [28].

Perissutti et al. developed the orally disintegrating tablets of Carbamazepine by melt granulation
technique. The granules were prepared by using polyethylene glycol (PEG-4000) as a melting binder and lactose monohydrate as hydrophilic filler without using solvents or water. The dissolution profiles of granules containing crosspovidone as an intragranulating agent were found to be superimposable to those prepared without it. Also, the extragranular addition of a small amount of crosspovidone gave rise to a further increase in disintegration rate and dissolution performances. [29].

Sublimation:
This technique is based on the use of volatile ingredients (e.g. camphor, ammonium bicarbonate, naphthalene, urea, urethane etc.) to other tablet excipients and the mixture is then compressed into tablets. Entrapped volatile material is then removed via sublimation, which leads to formation of a porous structure. These compressed tablets which have high porosity (approximately 30%) rapidly dissolved within 15 seconds in saliva. Several solvents like cyclohexane, benzene etc. can also be used as pore forming agents. Orodispersible tablets with highly porous structure and good mechanical strength have been developed by this method.

Koizumi et al. prepared highly porous compressed tablets. They used mannitol as a tablet matrix material while camphor as subliming agent. Camphor was removed by subliming in vacuum at 80°C for 30 minutes to develop pores in the tablets [30].

Makino et al. described a method of producing a fast dissolving tablet using water as a pore forming material. They used a mixture containing active ingredient and carbohydrates (glucose, mannitol, xylitol etc) which then moistened with water (1-3%w/w) and compressed into tablets. Then water was removed, yielding highly porous tablet [31].

Mass Extrusion
In this technique, a blend of active drug and other ingredients is softened using solvent mixture of water soluble polyethylene glycol, using methanol and then softened mass is extruded through the extruder or syringe to get a cylinder of product, which is finally cut into even segments with the help of heated blades to get tablets. The dried cylinder can be used to coat the granules of bitter tasting drugs and thereby masked their bitter taste [32].

Cotton Candy Process
This process utilizes a unique spinning mechanism to produce floss-like crystalline structure. Cotton candy process involves formation of matrix of polysaccharides or saccharides by simultaneous action of flash melting and spinning. The matrix formed is partially recrystallized to improve flow property and compressibility. This candy floss matrix is then milled and blended with active ingredients and excipients and subsequently compressed to orally disintegrating tablet. This process can accommodate larger drug doses and offers improved mechanical strength. However, high-process temperature limits the use of this process [33].

Direct compression
This is most popular technique because of its easy implementation and cost-effectiveness. The basic principle involves addition of disintegrants and/or water soluble excipients and/or effervescent agents. Superdisintegrants in optimum concentration (about 2-5%) are mostly used so as to achieve rapid disintegration along with the good mouth feel.

Bi et al. examined the disintegrant property of mixture of microcrystalline cellulose and low substituted hydroxy propyl cellulose (MCC: L-HPC) for orally disintegrating tablet and found that shortest disintegration time was observed in the range of ratio of MCC: L-HPC (8:2 to 9:1) [34].

Cousin et al. prepared orally disintegrating tablet using carboxymethyl cellulose as disintegrating agent and swelling agent consisting of modified starch or microcrystalline cellulose. The tablets disintegrate in the mouth in less than 60 seconds [35].

Gillis et al. prepared a fast-dissolving tablet of Galanthamine hydrobromide which comprise of diluent which is a spray dried mixture of lactose monohydrate and microcrystalline cellulose in the ratio of 75:25, a cross linked polymeric disintegrant such as crosspovidone and a direct compression process was used for preparation of fast dissolving tablets [36].

Gattani et al. prepared Ondansetron mouth dissolving tablet using treated agar as a superdisintegrating agent and found that tablets with treated agar powder had disintegration rate comparable to other superdisintegrants [37].

Patented technologies for orally disintegrating drug delivery system
The various technologies are developed for the preparation of Orally Disintegrating Drug Delivery System that are:

- Zydis
- Lyoc
- Wowtab
- FlashTab
- Durasolv
- Orasolv
- Frosta
- AdvaTab
- Flashdose
- OraQuick
- Nanocrystal Technology
- Quick-Dis Technology
- EFVDAS
- Fast Melt
- Multiflash

**Zydis® (Cardinal Health Inc.)**
Zydis® was first marketed technology and introduced by R. P. Scherer Corporation (Cardinal Health, Inc.) in 1986. Zydis tablet is produced by lyophilizing the drug in a matrix usually consisting of gelatin. The product is very lightweight and fragile and must be dispensed in a special blister pack. Zydis formulation is also self-preserved because the final water concentration in the freeze-dried product is too low to allow for microbial growth [21].

Disadvantages to the Zydis® technology-
- Relatively expensive & time consuming manufacturing process.
- Formulation is very lightweight and fragile.
- Poor stability at higher temperatures and humidity & stress conditions.
- A water insoluble drug can be incorporated only upto 400 mg per tablet or less. On the other hand water soluble drug can be incorporated only upto 60 mg.

The preferred drugs are water insoluble, low dose, chemically stable, small particle size and tasteless. The two most commonly used structural additives are gelatin and mannitol. Some other structural additives (e.g., starches, gums etc.) may be used depending on the properties of the active ingredient. The best physical characteristics are achieved by using a mixture of a water-soluble polymer and a crystalline sugar alcohol or amino acid. The polymer gives the strength and resilience while the crystalline component gives the hardness and texture. Polymers such as gelatin, dextran or alginites are added to impart strength during handling. These form a glossy and amorphous structure. Mannitol or sorbitol is added to impart crystallinity, elegance and hardness. Various gums may be added to prevent sedimentation of dispersed drug particles. Water is used as a medium to ensure the formation of a porous dosage form. Collapse protectants like glycine may be used to prevent shrinkage of dosage form during freeze drying and long-term storage. If necessary, suspending agents and pH adjusting agents may be used [21].

**Lyoc (Cephalon Corporation)**
Lyoc technique was owned by Cephalon Corporation. Lyoc utilizes a freeze drying process but differ from Zydis in that the product is frozen on the freeze dryer shelves. The liquid solution or suspension preparation evolves fillers, thickening agents, surfactant, non-volatile flavoring agents and sweeteners along with drug. This homogeneous liquid is placed in blister cavities and subjected to freeze drying. To prevent inhomogeneity by sedimentation during this process, these formulations require a large proportion of undissolved inert filler (mannitol), to increase the viscosity of the inprocess suspension. The high proportion of filler reduces the potential porosity of the dried dosage form and results in denser tablets with disintegration rates are comparable to loosely compressed fast melt formulations [38].

**Wowtab (Yamanouchi Pharma Technologies, Inc.)**
Wowtab technology was developed by Yamanouchi Pharma Technologies. ‘Wow’ means ‘without water’. The active ingredients may constitute upto 50% w/w of the tablet. Here, saccharides of both low and high Moldability are used to prepare the granules. Moldability is the capacity of a compound to be compressed. Highly Moldable substance has high compressibility and thus slow dissolution. The combination of high and low Moldability is used to produce tablets of adequate hardness & a rapidly melting strong tablet. Active ingredients are mixed with low Moldability saccharides and then granulated with high Moldability saccharides and then compressed into tablet. Wowtab product dissolves quickly in 15 s
or less. Wowtab product can be packed in both into conventional bottle and blister packs. This technology utilizes conventional granulation and tableting methods and used for both water-soluble and insoluble drugs. The manufacturing process involves granulating low-moldable sugars (e.g. mannitol, lactose, glucose, sucrose, and erythritol) that show quick dissolution characteristics with high moldable sugars (e.g. maltose, maltitol, and sorbitol). The result is a mixture of excipients that have fast-dissolving and highly moldable characteristics [1, 12].

**Flashtab (Prographarm)**
Flashtab was developed by Prographarm. A disintegrating agent and a swelling agent are used in combination with coated taste-masked microgranules of drug. FlashTab involves coating a drug with a Eudragit polymer to provide rapid release of the drug in the stomach, and formulating this microencapsulated drug with an effervescent couple to produce a flash dispersal tablet. This technology includes granulation of excipients by wet or dry granulation method followed by compression into tablets. Disintegrating agents include polyvinylpyrrolidine or carboxy methyl cellulose and Swelling agents include carboxymethylcellulose, starch, modified starch, microcrystalline cellulose, carboxy methylated starch etc. These tablets have satisfactory physical resistance. Tablets containing hygroscopic materials can also be blister packed using high quality polyvinyl chloride or aluminum foils for providing the higher degree of moisture protection than normal polyvinyl chloride or polypropylene foils [1, 12].

**Durasolv (Cima Labs, Inc.)**
DuraSolv is Cima's second-generation fast-dissolving/disintegrating tablet formulation. DuraSolv has much higher mechanical strength than OraSolv due to the use of higher compaction pressures during tableting. DuraSolv product is thus produced in a faster and more cost-effective manner. DuraSolv is so durable that it can be packaged in either traditional blister packaging or vials. This technology is not compatible with larger doses of active ingredients, because the formulation is subjected to such high pressures on compaction. Unlike OraSolv, the structural integrity of any taste masking may be compromised with high drug doses. The drug powder coating in DuraSolv may become fractured during compaction, exposing the bitter-tasting drug to a patient's taste buds. Therefore, DuraSolv technology is best suited for formulations including relatively small doses of active compound. The tablets made by this technology consist of a drug, fillers and a lubricant and prepared by using conventional tableting equipment and have good rigidity. These can be packed into conventional packaging system like blisters. Due to higher force of compaction used, tablets prepared are rigid [12].

**Orasolv (Cima Labs, Inc.)**
OraSolv® is Cima’s first orally disintegrating dosage form. It is based on direct compression of an effervescent agent and taste masked drug. The use of effervescence causes a tablet to disintegrate rapidly in less than 1 min on contact with water or saliva leaving coated drug powder. This technique is frequently used to develop over the counter formulations. This technology can accommodate a wide range of active ingredient from 1 mg to 500 mg. The effervescence occurs due to chemical reaction between organic acid such as citric acid, fumaric acid or maleic acid and a base such as sodium bicarbonate, potassium bicarbonate, magnesium bicarbonate, which result in generation of CO₂ [39, 40]. Effervescent disintegration agents evolve gas by means of chemical reaction called effervescent couple. Carbonates such as sodium bicarbonate, sodium carbonate, potassium bicarbonate and potassium carbonate, magnesium carbonate, and acids like citric, tartaric, fumaric, adipic and succinic are used. Microparticles, effervescent agents and other ingredient such as flavors, sweeteners, colorants and lubricants are blended and compressed at a low degree of compaction [40].

**Frosta (Akina)**
It utilizes the concept of formulating plastic granules and compressing them at low pressure to produce strong tablets with high porosity. Plastic granules composed of porous and plastic material, water penetration enhancer, and binder. The process involves mixing the porous plastic material with water penetration enhancer followed by granulating with binder. The tablets obtained have excellent hardness and rapid disintegration time ranging from 15 to 30 sec depending on size of tablet [41].

**AdvaTab (Eurand)**
In this technology, microencapsulation process is used for coating the drug particles with gastro soluble polymer so as to mask the taste along with restriction of drug dissolution in mouth cavity. AdvaTab tablets disintegrate rapidly in the mouth, typically in less than 30 seconds. These tablets are especially suited to those patients that experience difficulty in swallowing capsules and tablets. AdvaTab is distinct from other orally disintegrating tablet technologies as it can be combined with Eurand’s complimentary particle technologies like its world leading Microcaps® (taste-masking technology) and its Diffucaps® (controlled release technology) [41].

**Flashdose (Fuisz Technologies, Ltd.)**
This technology is patented by Fuisz. This uses the combination of Shearform and Ceform technologies in order to mask the bitter taste of the drug.
A sugar based matrix, called ‘Floss’, which is made up of a combination of crystalline sugars alone or in combination with drugs, is used. Floss is self binding shearform matrix, which is prepared by flash heat processing. FlashDose technology utilizes a unique spinning mechanism to produce a floss-like crystalline structure, much like cotton candy. This crystalline sugar can then incorporate the active drug and be compressed into a tablet. This procedure has been patented by Fuisz and is known as Shearform. It disperses and dissolves quickly. The method has certain drawbacks like the dosage form can accommodate only up to 600 mg of drug and tablets required specialized packing as highly friable, soft and moisture sensitive nature.
Instead of a floss-like material, small spheres of saccharides can be produced to carry the drug. The process of making microspheres has been patented by Fuisz, and is known as Ceform and serves as an alternative method of taste masking. Ceform technology involves preparation of microspheres of the active drug. Drug material alone or in combination with other pharmaceutical substances, and excipients is placed into a rapidly spinning machine. The centrifugal force comes into action, which throws the dry drug blend at high speed through small heated openings. Due to the heat provided by carefully controlled temperature, drug blend liquefies to form a sphere, without affecting the drug stability. The formed microspheres are compressed into tablet. This technique effectively masked the taste of product [12, 42, 43].

**OraQuick (KV Pharmaceutical Co., Inc.)**
OraQuick utilizes its own patented taste masking technology i.e. MicroMask®. In MicroMask® technology, taste masking process is done by incorporating drug into matrix microsphere. In this technique, tablet is prepared by dissolving the sugar (sucrose, mannitol, sorbitol, xylose, dextrose, fructose or mannose) and protein (albumin or gelatin) in a suitable solvent such as water, ethanol, isopropyl alcohol and ethanol-water mixture. The solution of matrix is then spray dried, yielding highly porous granules. Also, utilization of lower heat of production is advantageous for heat-sensitive drugs. Granules formed then mixed with drug and other excipients and compressed at low compression force. KV pharmaceuticals claimed that matrix formed protects and surrounds the drug powder in microencapsulated particles is more reliable during this step [44].

**Nanocystal Technology (Elan corporation)**
This technology is based on concept that decreasing particle size increases the surface area, which leads to an increase in dissolution rate. NanoCrystal particles are small particles of drug substance, typically less than 1000 nm in diameter, which are produced by wet milling the drug.
NanoCrystal™ fast dissolving technology provides for:
- Pharmacokinetic benefits of orally administered nanoparticles (<2 microns) in the form of a rapidly disintegrating tablet matrix.
- Product differentiation based upon a combination of proprietary and patent-protected technology elements.
- Cost-effective manufacturing processes that utilize conventional, scalable unit operations.
- Exceptional durability, enabling use of conventional packaging equipment and formats (i.e., bottles and/or blisters).
- Wide range of doses (up to 200mg of API per unit).
- Utilization of non-moisture sensitive inactives.
NanoCrystal colloidal dispersions of drug substance are combined with water-soluble GRAS (Generally Regarded as Safe) ingredients, filled into blisters, and lyophilized. The resultant wafers are remarkably
robust, yet dissolve in very small quantities of water in seconds. This approach avoids manufacturing operations (e.g., granulation, blending, and tableting) that generate large quantities of aerosolized powder and present much higher risk of exposure. The freeze-drying approach also enables small quantities of drug to be converted into orally disintegrating dosage forms because manufacturing losses are negligible [45].

**Quick-Dis Technology (Lavipharm)**
Lavipharm Laboratories Inc. has invented an ideal intraoral fast-dissolving drug delivery system called as Quick-Dis™. This is a thin, flexible, and quick-dissolving film. The film is placed on the top or the floor of the tongue. It is retained at the site of application and rapidly releases the active agent for local and/or systemic absorption. The Quick-Dis™ drug delivery system can be provided in various packaging configurations, ranging from unit-dose pouches to multiple-dose blister packages. Disintegration time is only 5 to 10 seconds for the Quick-Dis™ film with a thickness of 2 mm. The dissolving time, which is defined as the time at which not less than 80% of the tested film is dissolved in aqueous media, is around 30 seconds for Quick Dis™ film with a thickness of 2 mm. The typical release profile of an active ingredient exhibited by a Quick-Dis™ drug delivery system is 50% released within 30 seconds and 95% within 1 minute [46].

**EFVDAS (Elan Corporation)**
EFVDAS or Effervescent Drug Absorption System is a drug delivery technology that has been used in the development of a number of both OTC and prescription medications. This is particularly advantageous for conditions such as colds and flu, for which Elan has modified its EFVDAS technology to develop hot drink sachet products that combine medicines and vitamins for OTC use. The granular contents of the sachets can be added to boiling water to produce pleasant-flavored solutions. In these cases the effervescence of the granulate mixture is modified to accommodate the use of heated water. Examples of products that Elan has developed include effervescent ibuprofen, acetaminophen, cimetidine, naproxen, and acetaminophen and codeine combination product [47].

It is a highly porous, microfine matrix tablet. Once placed on the tongue, this matrix rapidly absorbs liquid and disintegrates. The drug, in a stabilized, size-reduced form to ensure optimal solubility, dissolves rapidly. The combination of a mild effervescent base and drug processing ensures that the dosage form goes into solution in approximately 15 to 30 seconds. The drug is released rapidly within the oral cavity, where it dissolves to form a drug solution that is then swallowed. This is particularly advantageous in cases like migraine where a fast onset of clinical effect is required. A portion of the drug solution may be absorbed locally in the oral cavity and therefore may avoid first-pass metabolism in the liver that limits the bioavailability of many drugs. The fast-melt system rapidly disintegrates in the oral cavity; hence, patients do not have to swallow a large cumbersome dosage form, which discourages many from taking their medication. Thus, the fast-melt dosage form combines the benefits of liquid formulations with those of a solid oral dosage form [47].

**Multiflash (Prographarm)**
Multiflash is a multi-unit tablet composed of coated microgranules and fast-disintegrating excipients. This multiparticulate tablet quickly disintegrates in the esophagus after being swallowed with a minimum amount of water. This tablet avoids mucosal adhesion, and coated pellets can match various dissolution rates [47].

**Conclusion**
Orally disintegrating dosage forms had satisfactorily solved the major problem of non-compliance for pediatrics and geriatrics which occur mainly because of swallowing difficulty. This dosage form has been formulated for existing drugs for extending the patent life of the drug and also for granting the new patent. Majority of drugs can be formulated as orodispersible tablets. The safety and efficacy profile of drugs in orodispersible tablet is same like their conventional tablet dosage form. Based on conventional techniques, new techniques are developed like Zydis, WowTab, Orasolv and many more, which leads to getting a patent and new market strategy for orodispersible tablets. This dosage form are gaining market share day by day and becoming a better choice of acceptance.
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